REMARKS/ARGUMENTS

Claims 1-10, 12, 22, 37-57, 203 and 204 are currently pending in the application. Claims 43 and 55 are hereby cancelled without prejudice. Claims 11, 13-21, 23-36, 58-202 and 205-213 have been withdrawn without prejudice because they are drawn to a non-elected invention. Applicants request that the Examiner confirm the pending claims because at page 2 of the Office Action, the withdrawn claims were incorrectly noted. Claims 22 and 53 have been amended for clarification purposes and for purposes of correcting typographical errors. Support for the amendment to claims 1, 22, 53, 203 and 204 is found throughout the Specification, as filed, and no new matter is presented by the amendment. The support for the paragraphs added to the specification is found in originally filed claims 122, 123, 166, 182, 186 and thus no new matter is presented by the amendment to the specification. Applicants respectfully request favorable consideration in light of the preceding amendments and following remarks.

Applicants respectfully request a three month extension of time to respond to the Office Action until August 13, 2004. A completed credit card authorization form for $475 for the three month extension is submitted herewith. Applicants hereby claim small entity status. It is believed that no other fees are due at this time. In view of the following remarks and amendments, applicant respectfully request a timely Notice of Allowance be issued in this case.

Claim Objections

The Office provisionally objected to claim 43 as being a substantial duplicate of claim 40. Claim 43 has been cancelled, thus obviating the rejection.

Claim Rejections under 35 U.S.C. § 112, First Paragraph

Claims 54 and 55 were rejected under 35 U.S.C. § 112, first paragraph, for failing to reasonably convey to one skilled in the relevant art that the inventors possessed the invention. Claims 1-10, 12, 22, 37-57, and 203-204 were rejected under 35 U.S.C. 112, first paragraph, for containing subject matter which was not described in the specification to enable one skilled in the art to make and/or use the invention.

The Office asserts that claim 54 lacks written description because the specification does not disclose any particular computer program, algorithm, or "statistical methodology," which may be interpreted to be a computer program, specifically describe a computer program or algorithm called SNIDE. Although, the Office points to pages 6, 26-28 and 30-31 of the specification as describing SNIDE, and admits that "[i]t is possible that the steps of pages 26-27 are computer-implemented." (internal quotes omitted).

Applicants respectfully submit that claim 54 meets the requirements of § 112, 1st paragraph, because it is adequately described in the specification. As the Office asserts, SNIDE is described at least on pages 6, 26-28, and 30-31 of the specification. As described in the specification, SNIDE is a method and this method may be implemented by code, also called SNIDE in the specification. The steps of the method implemented by the computer program SNIDE are described, for example, on pages 26-27 of the specification:

> The predictive nature of all disease causing mutation data has been incorporated into the computational method and system SNIDE (Single Nucleotide variation IDEntification), which predicts variants using the following steps: (1) input of each codon in a queried DNA sequence; (2) determination of each possible nonsynonymous mutation; (3) assignment of predictiveness to that mutation based on the identity of the wild-type and resultant codon; and (4) ranking of all predictiveness values to highlight the most probable mutations in the gene. All input sequences may be filtered for low complexity regions because such regions are expected to be highly variable and prone to many contraction and expansion polymorphisms with modest or negligible effects on health.

An example of the code to construct the computer program SNIDE is disclosed, for example, in paragraph 76:

> The SNIDE package may be an assembly of, e.g., three PERL scripts connected by UNIX c-shell (csh) that performs one or more of the following tasks: (1) parsing of either user-supplied GENEBANK or FASTA input files delineating the coding DNA to be analyzed; (2) calculation of expected point mutation probabilities according to a user-defined threshold (default = top 5% of all codon mutation classes); and (3) ranking of point mutation predictions by -value and generation of a tab-delimited file suitable for standard spreadsheet applications such as Excel.

Thus, one of skill in the art, which the Examiner admits is quite high, would be able to make and use a computer program SNIDE based on applicant's disclosure. Accordingly, applicants request the withdrawal of the rejection and allowance of the claim.

The Office further asserts that Claim 55 lacks written description because SNoop is only defined on page 6 of the specification and is not described elsewhere. Claim 55 has been cancelled without prejudice, thus obviating the rejection.

The Office asserts that claims 1-10, 12, 22, 37-57 and 203-204 are not enabled because neither the prior art nor the specification teaches how to obtain a variation or codon predictiveness matrix such that variations or polymorphisms may be predicted. Applicants traverse the rejection.

Applicants respectfully submit that claims 1, 203 and 204, as amended, are enabled by the specification and claims as originally filed. More specifically, these claims, as amended, recite:

> Claim 1. A method for predicting one or more locations of single nucleotide polymorphisms, comprising the steps of:
>
> obtaining a variation predictiveness matrix; and
>
> predicting one or more locations of single nucleotide polymorphisms of a nucleic acid sequence based on the variation predictiveness matrix.

> Claim 203. A computer program embodied on a computer readable medium for predicting one or more locations of variations, comprising:
>
> a code segment for creating variation predictiveness matrix from a nucleic acid dataset;
>
> a code segment for comparing a wild-type gene sequence with the variation predictiveness matrix; and
>
> a code segment for predicting one or more locations of variations in the wild-type gene sequence based on the comparison.

> Claim 204. A computer program embodied on a computer readable medium for predicting one or more locations of polymorphisms, comprising:
>
> a code segment for creating a codon mutation predictiveness matrix from a mutant gene dataset;
>
> a code segment for comparing a wild-type gene sequence with the codon polymorphism predictiveness matrix; and
>
> a code segment for predicting one or more locations of polymorphisms in the wild-type gene sequence based on the comparison.

The specification and claims as originally filed fully enable the claims and teach one of skill in the art how to make and use the invention. For example, paragraph [0021] of the specification states:

> A "variation predictiveness matrix" is defined herein as a table, list or mathematical matrix generated from empirical sequence data that describes the expectation of every possible base to base mutation class to occur in one or more sequences as calculated from that base usage and

> frequency in a mutation database. The variation predictiveness matrix is capable of quantifying and qualifying, independently or concurrently, the likelihood or frequency of a sequence change occurring in a given nucleic acid sequence and/or the likelihood or frequency that the sequence change will have an effect on function, for example, on gene expression, exon expression, translocations, conservative and non-conservative amino acid changes, transcription, translation, termination, secondary, tertiary or quaternary DNA, RNA or protein structure, protein-protein interactions, biochemical activity, cell transport, signal transduction, intra and extracellular messengers, methylation, shuffling, clustering, splicing, message stability, protein stability, post-translational modifications, and the like. The variation predictiveness matrix is generally a list, chart, table or matrix that contains a predictiveness value, that may include, e.g., the likelihood or frequency of a sequence or polymorphism change occurring in a given nucleic acid base in a sequence and/or the likelihood or frequency that the sequence or polymorphism change will have an effect on function. The predictiveness value may also incorporate other factors that affect the overall score, value or number assigned for the specific matrix. Furthermore, the user of the matrix may change the threshold value of the score assigned to a base using the predictiveness value to increase the accuracy of scan or determination of the likelihood that a change in the sequence, polymorphism or mutation will have an effect at a later stage, e.g., a nonsynonymous change in protein sequence.

In further support of enablement, the claims as originally filed specifically call out the steps of creating a polymorphism predictiveness value and the steps for creating a polymorphism predictiveness matrix.

> For example, see claims 122 and 186 below:
>
> Claim 122. A method for creating a polymorphism predictiveness value for use in a mutation predictiveness matrix, comprising the steps of: calculating the mutation frequency from a first codon to a second codon in a dataset of two or more mutant genes; and determining a polymorphism predictiveness value from the calculated mutation frequency.
>
> Claim 186. A method for creating a polymorphism predictiveness matrix, comprising the steps of: calculating the mutation frequency from a first codon to a second codon in a dataset of two or more mutant genes; determining a polymorphism predictiveness value from the calculated mutation frequency; and generating a codon polymorphism predictiveness matrix that correlates the frequency of a first to a second codon mutation with the polymorphism predictiveness value.

Applicants have added the text of claims 122, 123, 166, 182 and 186 to the specification to bolster the support. In contrast to the Examiner's assertion, the above quoted passages from the specification describe the steps for creating a polymorphism predictiveness value and for creating a polymorphism predictiveness matrix . Thus, the claims are fully enabled because one of skill in the art would understand from the disclosure how to create a polymorphism predictiveness value and how to create a polymorphism predictiveness matrix. Accordingly, Applicants request the withdrawal of the rejection and allowance of the claims.

Claim Rejections under 35 U.S.C. § 112, Second Paragraph

Claims 9-10, 22, 53 and 54-55 were rejected under 35 U.S.C. § 112, second paragraph for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Office asserts:

> Claim 9: No antecedent basis exists for "the dataset."
>
> Claim 22: The term "further adjusted" is unclear because it implies that the variation frequency was previously adjusted.
>
> Claim 53: The step or steps required to "affect" the method of claim 1 is unclear.
>
> Claim 54: It is unclear whether applicant intends claim 54 to limit the method of claim 1 to comprise further method steps; e.g. those of pages 26-27 or merely intends the steps of claim 1 to be computer-implemented, or intends the steps of claim 1 to comprise an algorithm, or intends some other limitation.
>
> Claim 55: "SNooP" is only defined on page 6 of the specification.

Regarding claim 9, sufficient antecedent basis exists for "the dataset" in line 3 of claim 8. As suggested by the Examiner, applicants intend claim 54 to further limit claim 1 by having the steps be computer implemented. Claims 22 and 53 have been amended herein in accordance with the Office's suggestions and claim 55 has been cancelled without prejudice. Reconsideration and withdrawal of the rejections under 35 U.S.C. § 112 are respectfully requested.

Conclusion

Applicants respectfully submit that claims 1-10, 12, 22, 37-57, 203 and 204, as amended, are fully patentable. Applicants respectfully request that a timely Notice of Allowance be issued in this case. If the examiner has any questions or comments, or if further clarification is required, it is requested that the examiner contact the undersigned at the telephone number listed below.

Respectfully submitted,

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I certify that this paper is being transmitted via facsimile to Technology Center 4700 at (703) 872-9306 under 37 CFR 1.8 on the date indicated above.

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